REMARKS

Reconsideration and withdrawal of the rejections of the application are respectfully requested in view of the amendment and remarks herewith, which place the application into condition for allowance.

I. STATUS OF CLAIMS AND FORMAL MATTERS

Claims 1, 3-5, 8, 10-15 and 17-32 are pending. Claim 1 has been amended. No new matter has been added.

Support for the claim amendments in claim 1 can be found on page 6, lines 5-6; page 7, lines 10 and 29 and page 9, lines 15-21.

It is submitted that these claims, as originally presented, were patentably distinct over the prior art cited by the Examiner, and that these claims were in full compliance with the requirements of 35 U.S.C. § 112. The amendments and remarks presented herein are not made for the purpose of patentability within the meaning of 35 U.S.C. sections 101, 102, 103 or 112. Rather, the amendments and remarks are submitted simply for clarification and to round out the scope of protection to which Applicants are entitled.

II. THE INVENTION

The invention relates to a transdermal system comprising:

a) a cover layer,

b) a polymer layer comprising

i) at least one immobilized droplet comprising at least one active ingredient dissolved or dispersed in the at least one immobilized droplet and

ii) a dried layer comprising at least one water-soluble polymer,

wherein the at least one immobilized droplet is emulsified or dispersed in the dried layer,

c) an optionally active-ingredient-containing adhesive layer, and

d) a protective layer,

wherein the at least one active ingredient solution or dispersion is not miscible with water and wherein the at least one active ingredient is adapted to be delivered in a surge upon the breakdown of the polymer layer.

The polymer layer is manufactured by emulsifying, for example, a solution or dispersion of one or more active ingredients in a non-volatile or sparingly volatile solvent in an aqueous solution or melt of a hydrophilic polymer. The emulsion is spread onto an intermediate film. As

the emulsion solidifies, liquid-filled pores, for example, form in the polymer layer. That layer is subsequently dried and produces a film in which the active ingredient solution/dispersion is present in immobilized droplets.

The presently claimed invention has the advantage that the water-soluble polymer of the polymer layer can be etched or dissolved by moisture on the skin. As a result, a complete breakdown of the polymer layer occurs and the active ingredient is then relieved and delivered to the skin of the patient in a surge. Since the polymer active ingredient layer can comprises one or more water-soluble polymers, the moisture on the skin has to penetrate into that layer and etch it or dissolve it in order to allow the active ingredient immobilized therein, for example in the form of emulsion droplets, to diffuse out. The breakdown of the polymer layer and consequentially, the timing of the surge-like release of the active ingredient, may be adjusted precisely by adjusting, for example, the loading, thickness, composition, pore size, and water-permeability of the polymer layer.

III. THE INVENTION IS DEFINITE

Claims 5 and 10 are rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. Independent claim 1 recited consisting language wherein the transdermal system can only contains four layers, however, dependent claims 5 and 10 recite two adhesive layers. Claim 1 has been amended to recite a transdermal system comprising the four layers, thereby obviating the rejection.

Consequently, reconsideration and withdrawal of the Section 112, second paragraph, rejection is believed to be in order and such actions are respectfully requested.

IV. THE INVENTION IS NOT ANTICIPATED AND/OR OBVIOUS OVER WO 95/24172, WO 89/07959 AND/OR U.S. PATENT NO. 5,242,391

Claims 1, 8, 10-12, 17-20, 28 and 30 were rejected under 35 U.S.C. §102(b) as allegedly being anticipated by WO 95/24172 and claims 1, 5, 8, 10-12, 17-20, 24, 28, and 30-31 were rejected under 35 U.S.C.§102(b) as allegedly being anticipated by WO 89/07959. Claims 13-15, 21-24, 26-27 and 29 were rejected under 35 U.S.C §103(a) as being allegedly unpatentable over by WO 95/24172; claims 13-15, 21-27 and 29 were rejected under 35 U.S.C.§103(a) as allegedly being unpatentable over WO 89/07959; claim 4 was rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over WO 95/24172 or WO 89/07959 in view of Wick et al. (U.S. Patent No. 5,679,373); claim 32 was rejected under 35 U.S.C. § 103(a) as allegedly being

unpatentable over WO 95/24172 or WO 89/07959 in view of Place et al. (U.S. Patent No. 5,242,391). These rejections will be collectively addressed and are respectfully traversed. None of the cited documents teach, suggest, enable or motivate a skilled artisan to practice the instant invention.

WO 95/24172 and WO 89/07959 do not teach or suggest the presently claimed invention.

WO 95/24172 relates to transdermal or transmucosal drug delivery (TDD) devices for the delivery of drugs, preferably heat sensitive or volatile drugs, such as, for example nicotine, to the skin or mucosal tissues. (See page 1, 1st paragraph). The TDD devices of the reference comprise a proximal and a distal adhesive layer (proximal or distal with respect to the skin/mucosal surface) laminated together and a drug-containing gel that is extruded therebetween (Id.). The reference teaches that the drug-containing gel is a liquid drug that is in a viscous yet flowable state, such that the drug is dissolved in a solvent, like ethanol or water, or a low-viscosity semi-solid that can be extruded, such as low molecular weight polymers, waxes, peteroleum jelly, and the like. (See page 8, 2nd full paragraph). WO 95/24172 purports that during operation, the drug contained in the extruded gel layer diffuses into one or both of the proximal and distal adhesive layers (See page 13, 2nd full paragraph and page 16, lines 9-17). The reference further suggests that after a period of equilibration, the drug becomes diffused thoughout the dual adhesive layers (see Id.) and stresses that the adhesive layer must not only be capable of absorbing the drug from the gel layer, but also capable of allowing it to diffuse from the adhesive to the skin or mucosa at an acceptable rate of flux. (See page 18, 2nd full paragraph).

WO 95/24172 does not teach, fairly suggest, or enable a polymer layer comprising (i) at least one immobilized droplet comprising at least one active ingredient dissolved or dispersed in the at least one immobilized droplet and (ii) a dried layer comprising at least one water-soluble polymer, wherein the at least one immobilized droplet is emulsified or dispersed in the dried layer. Further, WO 95/24172 does not teach, fairly suggest or enable a drug adapted to be delivered in a surge. Moreover, there is no motivation to modify the transdermal systems of either WO 95/24172 and WO 89/07959 to create the transdermal system of the presently claimed invention.

Instead, WO 95/24172 relates to a TDD device having a liquid-containing drug gel layer extruded between two adhesive layers. Nowhere does the reference teach, suggest, or enable the drug gel layer to be dried. In fact, the reference teaches away from drying the drug gel layer by stressing that the invention particularly relates to TDD devices for delivering heat sensitive or

volatile drugs as its manufacturing process does not include a drying step. In addition, WO 95/24172 does not teach or suggest or enable a surge-like delivery of an active substance. Quite the opposite, the device of WO 95/24172 appears to be in line with the prior art already described in the background of the instant application. In particular, the instant application points to prior art "matrix-type" TDD devices which are constructed to release an active substance purely based on diffusion through the device. Likewise and as noted above, WO 95/24172 teaches a TDD device with an active substance provided in a gel and which is extruded between two adhesive layers, and further which diffuses from the gel into the adhesive layers and then onto the skin or mucosa surface. Accordingly, Applicants respectfully assert that the presently amended claims are patentable over WO 95/24172.

WO 89/07959 relates to an occlusive body, such as a patch, a pad, or bandage, for the transdermal administration of a physiologically active substance by attachment to the skin or a buccal membrane at a controlled rate over an extended period of time. (See page 1, 1st paragraph). Indeed, the reference purports that an object of the invention is to provide a transdermal system in which the rate of delivery of the active substance is more nearly constant and/or in which the rate of delivery of the active substance is substantially constant over a greater proportion of the total dose contained in the drug reservoir of the device. (See page 6, top paragraph). More in particular, WO 89/079959 relates to an occlusive body (e.g. a patch, pad, or bandage) comprising a reservoir containing said active substance in liquid form and a filler material which stabilizes the reservoir contents. The wall of the reservoir comprises a microporous membrane which is permeable to and in contact with the active substance. The membrane is either hydrophobic, with the reservoir containing a hydrophilic wetting agent, or the membrane is hydrophilic, with the reservoir containing hydrophobic contents. (See page 6, 2nd full paragraph). The reference further purports that the active substance in the reservoir concentrates near the permeable membrane as a result of the mutual repulsion between the membrane and the reservoir material, which is stabilized by the filler, thus ensuring a steady rate of diffusion of the active substance through the membrane and onto the delivery surface.

WO 89/07959 does not teach, fairly suggest, or enable a polymer layer comprising (i) at least one immobilized droplet comprising at least one active ingredient dissolved or dispersed in the at least one immobilized droplet and (ii) a dried layer comprising at least one water-soluble polymer, wherein the at least one immobilized droplet is emulsified or dispersed in the dried layer. Further, WO 89/07959 does not teach, fairly suggest or enable a drug adapted to be

delivered in a surge. Moreover, there is no motivation to modify the transdermal system of WO 89/07959 to create the transdermal system of the presently claimed invention.

First, WO 89/07959 relates to a transdermal device comprising a reservoir and drug-permeable membrane, where the reservoir contains an active substance in a liquid form. Thus, unlike the present invention, the drug substance is not in the form of immobilized droplets of active ingredient which are emulsified or dispersed in a dried layer of a water-soluble polymer. WO 89/07959 simply does not teach or suggest such a feature and fails to point to any manufacturing step that would result in a dried polymer layer. Further, unlike the present invention, the device of WO 89/07959 does not provide a surge-like delivery of an active substance. Rather, the reference relates to the delivery of an active substance from a liquid-based reservoir through a permeable membrane at a rate that is constant. Indeed, WO 89/07959 is in line with the prior art description of membrane-type TDD devices as provided in the background section of the instant application, which "have been designed with the aim of providing a time-constant delivery of active ingredient." (See page 2, 2nd full paragraph). Accordingly, Applicants respectfully assert that the presently amended claims are patentable over WO 89/07959.

Wick et al. (U.S.5,679,373) and/or Place et al. (U.S. Patent No. 5,242,391) do not cure the deficiencies of WO 95/24172 or WO 89/07959, alone or in combination. The '373 patent relates to carrier layer of an active ingredient selected from active agent, active agent enhancers and mixtures thereof, melt-blended with a thermoplastic matrix polymer capable of controllably releasing the active ingredient, wherein the active ingredient is heat stable at the melt temperature of the matrix polymer. The '373 patent does not teach or suggest releasing active ingredients in a surge upon the breakdown of the layer containing the active ingredient.

The '391 patent relates to transurethral administration of the appropriate therapeutic drug(s) to treat erectile dysfunctions where the therapeutic agent is applied as a coating on a penile insert configured to prevent complete insertion and to facilitate removal or the agent is contained in a gel, cream, ointment or suppository for example which may be deposited in the urethra from a specially designed inserter. The '391 patent does not teach or suggest a transdermal system, such as a transdermal patch or matrix.

Neither U.S. patent teaches or suggests a polymer layer comprising (i) at least one immobilized droplet comprising at least one active ingredient dissolved or dispersed in the at least one immobilized droplet and (ii) a dried layer comprising at least one water-soluble

polymer, wherein the at least one immobilized droplet is emulsified or dispersed in the dried layer. Even if the references were combined, the combination does not teach or suggest the presently claimed invention.

Consequently, reconsideration and withdrawal of the Sections 102 and 103 rejections are believed to be in order and such actions are respectfully requested.

CONCLUSION

In view of the remarks and amendments herewith, the application is believed to be in condition for allowance. Favorable reconsideration of the application and prompt issuance of a Notice of Allowance are earnestly solicited. The undersigned looks forward to hearing favorably from the Examiner at an early date, and, the Examiner is invited to telephonically contact the undersigned to advance prosecution. The Commission is authorized to charge any fee occasioned by this paper, or credit any overpayment of such fees, to Deposit Account No. 50-0320.

Respectfully submitted,

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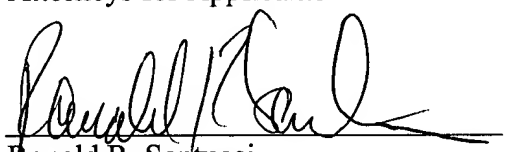
By: 

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